REMARKS

Applicants note with appreciation the Examiner's acknowledgment of the Applicants' election of Group IV. Applicants of course reserve the right to pursue the non-elected inventions in one or more divisional applications.

Applicants respectfully submit that Claims 96 and 97 should be examined on the merits, in as much as the claims refer specifically to SEQ. ID No. 5 and further, that the examination of both claims would not present a burden on the Examiner. Applicants respectfully submit that until the current Official Action, the Applicants had not received any actions on the merits for the current claims, and as a result, Claims 96 and 97 can be appropriately examined. The Examiner's attention is respectfully invited to §810 of the Manual of Patent Examining Procedure (hereinafter MPEP), which discusses when an action on the merits has been given. Specifically, the MPEP states that "In general, in an application when only a written requirement to restrict is made, no action on the merits is given." In view of this well established principle the Applicants respectfully request that the Examiner consider Applicants' Claims 96 and 97.

Claim Rejections Under 35 U.S.C. § 112

Claim 95 has been rejected under 35 U.S.C. § 112, second paragraph. Applicants have amended Claim 95 to remove the term "represented" and made further amendments to help define the claim.

Claim 95 has been rejected under 35 U.S.C. § 112, first paragraph for containing subject matter which was not described in the specification in such a way to convey to one skilled in the art that the Applicants were in possession of the claimed invention. Applicants respectfully submit that in view of the claim amendment, and in further view of the remarks set forth below, the rejection is

now obviated.

The Applicants submit that as a result of the claim amendments, Claim 95 recites the structural and functional character of SEQ. ID No. 5 and/or the functional equivalents thereof. Support for the claim amendment may be found on page 39, lines 8-10; page 28, line 1 to page 29, line 6; and page 19, line 23 to page 20, line 3. As a result, no new matter has been added.

Turning to the objection to the use of "functional equivalents", the Applicants invite Examiner's attention to page 27-29 of the Applicants' Specification, wherein the term "functional equivalents", and the methods of obtaining functional equivalents is succinctly articulated. That passage states:

> In so far as the retrovirus binding domain and/or target cell binding domain which can achieve gene transfer with the high efficiency as described herein are maintained, the functional material to be used may be those having mutation in amino acid sequences of naturally occurring polypeptides. In the present invention, even if deletion, substitution, insertion and/or addition of one or plural, for example, up to several amino acids are present in the amino acid sequences of naturally occurring polypeptides, in so far as the desired retrovirus binding domain and/or target cell binding domain are maintained, such polypeptides are referred to as functional equivalents of the polypeptides having naturally occurring amino acid sequences. These functional equivalents can be obtained by preparing genes encoding the functional equivalents to produce the equivalents and ascertaining their biological activities.
>
> In this regard, the pertinent biotechnology arts have already advanced to a state in which the deletion, substitution, addition or other modifications of amino acids in the required functional domains can be routinely carried out. Then, the resultant amino acid sequences can be routinely screened for the desired cell binding activity or virus binding activity.
>
> A gene encoding the functional equivalent can be obtained by searching for genes hybridizable to the gene encoding the above functional material.
>
> That is, the gene encoding the above functional material or a part of

> its nucleotide sequence can be used as a probe of hybridization of primers of a gene amplification method such as PCR or the like to screen a gene coding a protein having a similar activity to the functional material. Sometimes, in this method, a DNA fragment containing only a part of the desired gene is obtained. In such case, after ascertaining that the resultant DNA fragment is a part of the desired gene, the whole desired gene can be obtained by carrying out hybridization with the DNA fragment or a part thereof as a probe or carrying out PCR with primers synthesized based on the nucleotide sequence of the DNA fragment.
>
> The above hybridization can be carried out, for example, under the following conditions.
>
> That is, a membrane on which DNA is immobilized is incubated in 6 x SSC (1 x SSC: 0.15M NaCl, 0.015M sodium citrate, pH 7.0) containing 0.5% of SDS, 0.1% of BSA, 0.1% of polyvinyl pyrrolidone, 0.1% of Ficoll 400 and 0.01% of denatured salmon sperm DNA together with a probe at 50°C for 12 to 20 hours. After completion of incubation, the membrane is washed with, firstly, 2 x SSC containing 0.5% of SDS at 37°C and then with changing the concentrations of SSC to 0.1 x SSC and temperatures to 50°C until the signal derived from the immobilized DNA can be distinguished from the background.

The Examiner's attention is further invited to page 69, line 3 to page 70, line 2, wherein the Applicants explain specific methodologies designed for the preparation of the isolated and purified polypeptide of SEQ. ID No. 5, which the Applicants have named C-FGF-CS1. In view of the detailed teachings contained in the Applicants' Specification, it is respectfully submit that one skilled in the art could readily identify a functional polypeptide having both a viral and target cell adhesion domain on one molecule, wherein the molecule functions to efficiently transfer a gene into a target cell.

Response to § 102 Rejection

Claim 95 has been rejected under 35 U.S.C. § 102(b) as being anticipated by Hashi et al. (1994). Applicants respectfully submit that a careful study of SEQ. ID No. 5 illustrates a structurally

and functionally different polypeptide than the polypeptide disclosed in Hashi et al.

Anticipation requires that the prior art reference teach each and every element of the Applicants claimed invention. Thus, failure to teach one of the Applicants' claim limitations requires a finding of no anticipation under 35 U.S.C. § 102.

The Examiner's attention is invited to amino acid residue 431 disclosed in Hashi et al., as compared with residue 431 of the Applicants' claims. A comparison of the two residues reveals that Hashi et al., has lysine at residue 431, while the Applicant shows alanine at residue 431. Consequently, the second lysine on the C-terminal of the Hashi et al. sequence is substituted with alanine in residue 431 of the Applicants' (SEQ. ID No. 5). Alanine is non-polar, and extremely hydrophobic, whereas lysine is a positively charged and extremely hydrophilic. The complete difference in hydrophobicity, coupled with the 431 residue's terminal location can cause significant secondary and tertiary structural differences between the two proteins.

Another significant difference between Applicants' sequence and the one disclosed in Hashi et al., is the Applicants' additional residues from 433-457 of (SEQ ID No 5). Specifically, the Examiner's attention is invited to page 127 of the Applicants' Specification, wherein the Applicants disclose SEQ. ID No. 2, which is identical to the sequence disclosed in residues 433-457 of SEQ. ID No. 5. Applicants respectfully submit that this 25 amino acid sequence, which comprises the terminal portion of SEQ. ID No. 5, provides the Applicants' SEQ. ID No. 5 with vastly different structural and functional properties as compared to that sequence disclosed by Hashi et al. The additional 25 amino acids correspond to CS-1 which is consistent with the portion of the IICS binding domain of human fibronectin. The domain exhibits the ability to bind hematopoietic cells, and thus, participate in cell-adhesion for the molecule. Nowhere, in Hashi et al. is there a discussion of a fibronectin fragment exhibiting the cell-adhesion property disclosed by the Applicants.

Specifically, this 25 amino acid sequence (CS-1), which as stated above is the cell-adhesion region derived from fibronectin, has been shown to be useful for gene transfer into cells. It is the addition of these extra 25 amino acids that has allowed for the increased efficiency of gene transfer into target cells. Withdrawal of the 35 U.S.C. § 102 rejection of Claim 95 is respectfully requested.

In view of the foregoing, Applicants respectfully submit that the Application is now in condition for allowance, which action is respectfully requested.

Respectfully submitted,

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